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using a CuKα ray, of about 6.0° until its water content is reduced to less than 3% by weight.

REMARKS

Claims 1-15 are pending in the present application.

Applicants wish to thank Examiners Zucker and Wilson for the helpful discussion with the Applicants' undersigned representative on February 26, 2001, and for the indication of the likely withdrawal of the rejection of Claim 2 under 35 U.S.C. §102.

The rejection of Claim 2 under 35 U.S.C. §102 over Nofre et al is respectfully traversed.

In maintaining this ground of rejection, the Examiner asserts that the Applicant has demonstrated that "Nofre et al discloses Neotame having a water content of 1.4%" in paragraph 6, on page 2, of the Declaration under 37 C.F.R. §1.132 (page 3, paragraph 5(a) of the Official Communication mailed December 4, 2002). Applicants submit that this assertion is without merit.

The Declaration does not disclose any Neotame *crystals* (A- or C-type) having a water content of 1.4% by weight, much less demonstrate that Nofre et al disclose Neotame crystals of less than 3% by weight. In paragraph 6 of the Declaration, the Applicants show that the Neotame powder obtained by the process described therein is "*an amorphous product which did not show a clear diffractive X-ray pattern.*" In the process of preparing Neotame, Nofre disclose of a gummy precipitate that is obtained prior to recrystallization (column 7, line 47). In order to obtain actual crystals (A-type), Nofre et al disclose that the gummy precipitate is filtered off, dried under vacuum and

recrystallized from an ethanol/water mixture or from acetonitrile (column 7, lines 47-51). Similarly, the amorphous product in paragraph 6 of the Declaration is obtained *without* recrystallization. Much in the same fashion as the gummy precipitate, the amorphous product serves as a purification intermediate. Therefore, this *non-crystalline*, amorphous product would be analogous to the gummy precipitate described by Nofre et al.

Moreover, Nofre et al do not disclose or suggest obtaining a C-type crystal (<3% water by weight) by drying an A-type crystal (3-6% water by weight) until the water content is reduced to less than 3% by weight. In fact, Nofre et al do not themselves realize the benefits afforded by the present invention as evidenced by their own subsequent patent, a copy of which is appended herewith and listed on Form PTO-1449 for the Examiner's convenience (listed as Claude et al, US Patent No. 5,510,508 issued April 23, 1996). In this later patent, which demonstrates the state of the art at the time of the present invention, Claude et al disclose that the water content of Neotame should be 3 to 6% (column 5, line 26). Therefore, in the absence of a disclosure of a crystal of Neotame containing less than 3% water by weight, the invention as claimed in Claim 2 is not anticipated by Nofre et al, and as such Applicants respectfully request withdrawal of this ground of rejection.

The rejection of Claim 1-15 under 35 U.S.C. §103 over Wakamatsu et al in view of Nofre et al is respectfully traversed.

Nofre et al, as discussed above, disclose Neotame (column 1, lines 7-9). Wakamatsu et al disclose a process for producing dry Aspartame having an improved solubility from wet crystals (Abstract). According to the method of Wakamatsu et al, wet Aspartame crystals are dried via a multi-step process to obtain crystals with a water

content of less than 5% by weight (Abstract). Wakamatsu et al further disclose that there are two types of Aspartame crystals, I and II type crystals, with the II type crystals having a lower hygroscopicity and stability when compared with the I type crystals (column 1, lines 22-27).

The Examiner asserts that it would be obvious to the skilled artisan to combine the teachings of Wakamatsu et al and Nofre et al to arrive at the present invention. The Examiner justifies his asserted combination on the basis of structural similarity of Neotame and Aspartame and the overlap in their intended uses (page 6, lines 1-3 of the Official Communication mailed December 4, 2002). In addition, the Examiner states the motivation to combine would "have been to provide the same improved solubility for neotame that the process of Wakamatsu provided for its close analog Aspartame" (page 5, lines 20-22 of the Official Communication mailed December 4, 2002). However, Applicants disagree with this assertion.

The present invention provides crystals of Neotame (C-type crystal), having a characteristic X-ray diffraction peak at a diffraction angle, 2θ, measured using a CuKα ray, of about 7.1°, which possess improved solubility (Claim 1). The C-type crystal is obtained by drying the less soluble A-type crystal until its water content is reduced to less than 3% by weight (Claim 2 and page 3, lines 13-19). In contrast, Wakamatsu et al state: "Aspartame maintains the crystal form having an excellent solubility (the I type crystal form) till the water content is reduced to about 15% by weight. The conversion from the I type to the II type takes place at a water content range of from 5 to 15% by weight" (column 2, line 35-40). Therefore, the novel C-type Neotame crystal is the exact inverse of what would be expected based on "its close analog" Aspartame, which undergoes a

transition from a more soluble (I type) crystal-state to a less soluble (II type) crystal-state under the same drying conditions.

Furthermore, the objective of Wakamatsu et al is to prevent such a transition from I type crystals to II type crystals during the drying process. Again, this is fundamentally different from the present invention in which C-type Neotame crystals are obtained through the A-type crystals by drying the A-type crystal until its water content is reduced to less than 3% by weight (Claim 2 and page 3, lines 13-19). Wakamatsu et al and Nofre et al provide no disclosure or suggestion of drying a less soluble crystal of Neotame (or Aspartame) to obtain a more soluble crystal by reducing the water content to less than 3% by weight. In the absence of such a disclosure or suggestion, the present invention would not be obvious to the skilled artisan based on Wakamatsu et al in view of Nofre et al.

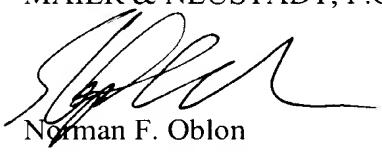
The rejection of Claims 1-2 under 35 U.S.C. §112, second paragraph, is obviated by amendment. Withdrawal of this rejection is requested.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



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Please amend the claims as follows:

--1. (Twice Amended) A crystal of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine methyl ester showing a characteristic X-ray diffraction peak at a diffraction angle [(2θ, CuKα ray)], 2θ, measured using a CuKα ray, of about 7.1°.

2. (Twice Amended) A process for producing the crystal according to claim 1, which comprises drying N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine methyl ester showing a characteristic X-ray diffraction peak at a diffraction angle [(2θ, CuKα ray)], 2θ, measured using a CuKα ray, of about 6.0° until its water content is reduced to less than 3% by weight.--

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